IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	**MDL Docket No. 4:03CV1507 WRW**
PREMPRO PRODUCTS LIABILITY LITIGATION	***Reeves v. Wyeth*, Case No. 4:05-cv-00163 WRW** ***Rush v. Wyeth*, Case No. 4:05-cv-00497 WRW**

REPLY IN SUPPORT OF WYETH'S
MOTION TO EXCLUDE EXPERT TESTIMONY
OF DR. DONALD F. AUSTIN

Dr. Austin's proposed testimony runs afoul of the *Daubert* criteria concerning reliability because his "what if" study is not something that epidemiologists do. The Court need never reach the reliability criteria, however, for Dr. Austin's testimony also strikes out against the more basic *Daubert* requirement that the testimony be relevant to the case. It is not relevant, because it covers a type of cancer that neither Plaintiff developed.

A. Dr. Austin's Testimony About Lobular Cancer Is Irrelevant Because Neither Ms. Reeves nor Ms. Rush Was Diagnosed with Lobular Cancer.

To be admissible, expert testimony must concern, or "fit," the facts of the particular case, because "[e]xpert testimony which does not relate to any issue in the case is not relevant and, ergo, non-helpful" to the jury.[1]

1. Plaintiffs concede that they were not diagnosed with lobular cancer.

Dr. Austin's report addresses one specific question: "If the available national cancer data had been monitored for changes in breast cancer incidence, could an increase in ILC [invasive

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[1] *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 591 (1993) (quotation omitted); *see Concord Boat Corp. v. Brunswick Corp.*, 207 F.3d 1039, 1055 (8th Cir. 2000) ("In recent years the Supreme Court has put renewed emphasis on the importance of the 'fit' of an expert's opinion to the data or facts in the case[.]") (*citing Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

lobular cancer] have been detected, and if so, when?"[2] As Dr. Austin's co-author testified, the question that he and Dr. Austin were "asked to answer [by Plaintiffs'counsel] was at what time in the past an increase in [lobular cancer] could have been detected."[3] Perhaps their question will be relevant for a future case, when the plaintiff has lobular cancer. But neither Ms. Reeves nor Ms. Rush had lobular cancer. Accordingly, Dr. Austin's opinions about lobular cancer are irrelevant and inadmissible.

2. Plaintiffs' reinvention of Dr. Austin's opinions has no basis in his report or testimony.

Faced with the fact that neither Ms. Reeves nor Ms. Rush had lobular cancer, the Opposition invents a new theory that has no basis in Dr. Austin's report or testimony. Plaintiffs contend that hormone therapy "causes hormone dependent breast cancers," which they assume are the same as estrogen-receptor-positive ("ER-positive") breast cancers.[4] And, according to Plaintiffs, the reason that Dr. Austin selected lobular cancer as the type of breast cancer to study is "because SEER did not collect data on hormone receptor status until 1990 [and] ILC was the most logical cell type to examine because it is hormonally the most sensitive."[5]

But Dr. Austin said no such thing in his report or in his testimony. Nowhere in Dr. Austin's lengthy explanation of his "simulated" monitoring program does he testify that he

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2 Austin Rep. (App., Ex. 2) at i.

3 Buckley Dep. (excerpts attached as Ex. 1) at 78.

4 Plaintiffs' Opposition to Wyeth's Motion to Exclude Expert Testimony of Dr. Austin (June 29, 2006) [*Reeves* Docket No. 136; *Rush* Docket No. 203) ("Pl. Opp.") at 11. Estrogen receptors are a part of a cell that responds to estrogen.

5 *Id.* at 5, 10.

monitored lobular cancer in order to detect ER-positive breast cancers. The reason Dr. Austin "did not examine all of the cell types" reported in the SEER database was because the research question was "whether monitoring those cell types would have detected an anomalous increase ***in ILC***, and, if so, when?"[6] That has nothing to do with Plaintiffs' ductal cancers.

3. Dr. Austin's testimony about lobular cancer is also irrelevant because it is not clinically significant.

Even if a study about lobular cancer risk were somehow relevant to the subject matter of these cases, Dr. Austin's testimony would still be irrelevant because, as shown in our opening brief,[7] there is no evidence that information about the differing risk among different breast cancer cell types—as opposed to the overall risk of breast cancer—would matter to doctors in prescribing hormone therapy. Dr. Buckley, Dr. Austin's co-author, conceded that such information was ***not*** important to him as a prescribing physician.[8] As if this is all an academic exercise, Plaintiffs assert that "what physicians would have done" with information about ILC does not matter.[9] But, if information about ILC is not important to the doctors who prescribe hormone therapy, then it is not relevant in this lawsuit. The issue here is not whether Wyeth could have contributed more to the general knowledge of the scientific community.

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6 Austin Rep. at i (emphasis added).

7 Memorandum in Support of Wyeth's Motion to Exclude Expert Testimony of Dr. Austin (June 5, 2006) [*Reeves* Docket No. 92; *Rush* Docket No. 149] ("Mem.") at 11-12.

8 Buckley Dep. at 259.

9 Pl. Opp. at 12.

B. Dr. Austin's Testimony Does Not Satisfy Any of the *Daubert* Factors.

Opinion developed for litigation. Plaintiffs concede that "Dr. Austin conducted his analysis for litigation."[10] That is a "very significant" factor in the *Daubert* analysis, and one weighing in favor of excluding Dr. Austin's testimony.[11] Only last month, the Eighth Circuit affirmed exclusion of expert testimony because, *inter alia*, "the theory was formulated in connection with . . . litigation."[12] Nor do Plaintiffs deny that Dr. Austin ***changed*** his opinion after meeting with Plaintiffs' counsel. The fact that his opinion bends to the will of counsel by itself demonstrates that it is not grounded upon any reliable methodology.

No testing. Dr. Buckley admitted that this study was not guided by any objective standard and was not tested.[13] Indeed, the very nature of this counter-factual inquiry—"could an increase in [lobular cancer] have been detected [in the past], and if so, when"—makes the results of the research untestable. The allegedly similar studies Plaintiffs cite (Glass/Hoover and Li) did not attempt to determine when an increase in lobular cancer could have been detected or to extrapolate such an increase to an association between hormone therapy and ductal cancer.

No peer review. Plaintiffs admit that Dr. Austin's study has not "been submitted for publication,"[14] another significant *Daubert* factor.[15] While ***counsel*** argues that there are similar studies, Dr. Buckley admits that he has not seen any peer-reviewed study.[16]

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[10] *Id.* at 15.

[11] *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995).

[12] *Wagner v. Heston Corp.*, __ F.3d __, 2006 WL 1549004, at *2 (8th Cir. June 8, 2006).

[13] Buckley Dep. at 236, 272-74.

[14] Pl. Opp. at 14.

[15] *Wagner*, 2006 WL 1549004, at *2.

Unknown rate of error. A standard-less study that cannot be tested or replicated plainly has an unknown, and unknowable, rate of error.[17]

No general acceptance. Plaintiffs argue that "[e]pidemiologists routinely do ecological studies,"[18] a statement that is a bit like saying that historians write political histories. Indeed they do, but they do not (except for sport) write counter-factual histories of the sort that begin "what if the British had won the Revolutionary War?" There is no (i) evidence that epidemiologists routinely attempt to re-create history by attempting to determine when an alleged association might have been known, (ii) no precedent for admitting such studies in court on a claim that a prescription drug caused a disease, (iii) and no basis for concluding that scientists generally accept such a study as evidence of ***anything*** when its own author admits that no known risk factor for the disease was taken into account.[19] Even if an increase in the rate of ILC were somehow relevant to this case, which it is not, given the latter admission there was no reason for Wyeth to investigate the issue at the time.

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[16] Buckley Dep. at 39.

[17] *See, e.g.*, *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1321 (11th Cir. 1999) ("Because the untested theories of Allison's experts are not generally accepted . . . they obviously have a high potential rate of error"); *Brumley v. Pfizer Inc.*, 200 F.R.D. 596, 602 (S.D. Tex. 2001) (because expert's opinion that Viagra causes heart attacks failed the first two *Daubert* factors, "the Court cannot assess the 'known rate of error' for a theory that has no empirical foundation").

[18] Pl. Opp. at 1.

[19] Austin Dep. (App., Ex. 1) at 168.

C. Dr. Austin's Opinions, even as Reformulated by the Opposition, Are Unreliable.

Even if Dr. Austin had expressed the opinion that hormone therapy "causes hormone dependent breast cancers" and ER-positive breast cancers are "hormone dependent"[20]—which he did not—that opinion is not reliable under *Daubert* according to the testimony of Plaintiffs' own expert, Dr. V. Craig Jordan. "Nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply ***too great an analytic gap*** between the data and the opinion proffered."[21]

1. Breast cancer can be ER-positive or ER-negative regardless of the person's sex, and regardless of a woman's hormone therapy use.

Dr. Austin's new opinion (if it is his opinion) makes a leap that Dr. Jordon says cannot be made. Most tumors are ER-positive, regardless of whether the person ever used hormone therapy.[22] Women who never took hormone therapy develop ER-positive tumors and, indeed, the vast majority of male breast cancers are ER-positive.[23] Similarly, women who took hormone therapy sometimes develop ER-negative tumors.[24] Thus, breast cancer can be ER-positive or

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[20] Pl. Opp. at 11.

[21] *Gen. Elec. Co.*, 522 U.S. at 146 (emphasis added); *see Concord Boat*, 207 F.3d 1055 (*quoting Gen. Elec. Co.*); *Jaurequi v. Carter Mfg. Co.*, 173 F.3d 1076, 1082 (8th Cir. 1999) (same).

[22] Jordan Dep. (excepts attached as Ex. 2) at 291.

[23] *Id.* at 284. According to an article cited in Plaintiffs' brief, from 1992 to 2001, 78% of ductal cancers reported in SEER were ER+ and 92% of lobular cancers were ER+ in women diagnosed at 50-89 years of age, which is contrary to Plaintiffs' contentions that ILC is "always hormone receptor positive" and that "a significant percentage of ductal cancers are ER negative." Pl. Opp. at 10 & n.24 (Li study).

[24] Jordan Dep. at 287.

ER-negative regardless of whether the person took hormone therapy (and regardless of sex). Dr. Jordan admitted that the WHI study found no difference in the incidence of ER-positive tumors between women treated with hormone therapy and women who received a placebo.[25]

2. ER-positive tumors are not necessarily stimulated by estrogen.

Dr. Austin's new opinion assumes that ER-positive tumors are "hormone dependent" and that "the hormones in CMHT made [Plaintiffs' tumors] grow."[26] First, it is not necessarily the case that ER-positive tumors are stimulated by estrogen. Dr. Jordan testified that half of ER-positive tumors are "estrogen independent."[27] Second, even if an ER-positive tumor is stimulated by estrogen (and there is no way to know if it is), post-menopausal women produce enough endogenous estrogen in their bodies to cause the tumor to grow even if they never took hormone therapy. As Dr. Jordon acknowledged:

> Q: . . . in the post-menopausal woman, her own endogenous hormones can still cause this occult breast cancer to proliferate or grow?
>
> A: In the absence of any more estrogen, that is correct.[28]

So, again, this new opinion makes a leap that is unsupported by the wisdom, according to Plaintiffs' other expert.

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[25] *Id.*

[26] Pl. Opp. at 1, 11.

[27] Jordan Dep. at 185-86.

[28] *Id.* at 68.

3. The SEER data is inconsistent with the hypothesis that hormone therapy is responsible for an increased incidence of ER-positive breast cancers.

In 2003, Dr. Jordan wrote an article criticizing a study that used SEER "to illustrate that the proportion of hormone receptor positive tumors is rising . . . [and] conclude[] that this implicates hormonal factors, primarily an increased use of hormone replacement therapy (HRT)."[29] Dr. Jordan stated that:

> [I]f the primary cause for the phenomenology was HRT, one would anticipate significant increases in ER-positive status in only 50- to 59- or 60- to 69-year-olds, who are most likely to be taking HRT. This was not observed, as the strongest trend toward an increased incidence of ER-positive tumors was noted in 40- to 49-year-olds, who were most likely to be premenopausal.[30]

Dr. Jordan's criticism of using the SEER database for this type of study echoes many of the criticisms Wyeth has made of Dr. Austin's study. For example, in the late 1980s and early 1990s, laboratories changed the methodology used to determine hormone receptor status, and, as Dr. Jordan and others have pointed out, these changes in testing protocol could alone account for the observed increase.[31]

If the touchstone of Rule 702 and *Daubert* is reliability, then surely Plaintiffs cannot offer a theory that is criticized at every turn by another of Plaintiffs' experts.

CONCLUSION

For the foregoing reasons, Wyeth respectfully request that the Court exclude the expert testimony of Dr. Austin.

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[29] V. Craig Jordan, *The Ups and Downs of the Estrogen Receptor*, Journal of Clinical Oncology (January 1, 2003) at 3 (attached as Ex. 3); *see also* Jordan Dep. at 272-74.

[30] Jordan, *supra*, at 3; *see also* Jordan Dep. at 276-77.

[31] Jordan Dep. at 275.

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CERTIFICATE OF SERVICE

I hereby certify that on this 10th day of July 2006 a true and correct copy of the foregoing Reply Memorandum in Support of Wyeth's Motion to Exclude Expert Testimony of Dr. Austin was electronically filed with the Clerk of Court using the CM/ECF system and a true and correct copy was forwarded by e-mail and first-class mail, postage prepaid, to the parties listed below.

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